Case Report

Anti-retroviral therapy's miracle in the treatment of Bowen's disease in a human immunodeficiency virus-positive patient: A rare case report

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Abstract

Bowen's disease (BD) is a form of squamous cell carcinoma *in situ* often associated with human papillomavirus. Co-infection with human immunodeficiency virus (HIV) is associated with a greater risk of malignancy. We describe a case of BD in a 52-year-old unmarried HIV-positive male who presented with extensive skin lesions of 1-year duration. Histopathology was suggestive of BD. He had been tried with topical imiquimod cream and cryo-therapy for 6 months. We observed no response for these above therapies. He was started on with anti-retroviral therapy (ART) as his CD4 count was 253 cells/mm^3. The entire cutaneous lesions completely disappeared within 6 months of ART, which was an interesting incidence.

Key words: Anti-retroviral therapy, Bowen's disease, human Immunodeficiency virus

INTRODUCTION

Bowen's disease (BD) is a rare, persistent, progressive intra-epidermal carcinoma, which may be potentially malignant, with up to 8% of the cases progressing to squamous cell carcinoma (SCC).[1] The various treatment modalities include physical destruction using electrocautery, cryotherapy, curettage, laser therapy or surgical excision, intralesional interferon alpha or bleomycin, and noninvasive methods such as photodynamic therapy and topical 5-fluorouracil.[1] Here, we report a case of multiple BD in an immunosuppressed seropositive adult patient which completely resolved with anti-retroviral therapy (ART) which is a very rare event.

CASE REPORT

A 52-year-old unmarried male, human immunodeficiency virus (HIV)-positive since 2006 presented in August 2014 with slowly progressive asymptomatic skin lesions all over the body of 1-year duration. He gave a history of Siddha treatment for his immunodeficient state during the year 2007-2008 for 1 year. However he was unable to tell the details of his treatment. Systemic examination was normal and vitals were stable.

Dermatological examination showed multiple, discrete, reddish-brown-colored, 1-1.5cms papular and nodular lesions with crusting on the chest, back, and both thighs [Figures 1 and 2]. Except for palpable inguinal nodes on both sides, examination of external genitalia was normal. Mucosae were normal and there was no other clinical evident sign suggestive of chronic arsenic ingestion.

All his hematological and biochemical investigations were within normal limits. His chest X-ray and ultrasound examination of the abdomen were normal. A skin biopsy was done from the right thigh

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lesion, and histopathological examination (HPE) showed hyperkeratosis, parakeratosis, and dyskeratosis with marked acanthosis [Figure 3]. Epidermis showed atypical cells and moderate to severe dysplasia with intact basement membrane [Figure 4]. From the above HPE findings, a diagnosis of BD was made. As his CD4 count was 380 cells/mm^3, ART was not started. He was treated initially with topical 5% imiqumod cream for 3 months. As there was no response, he was treated with cryotherapy for the next 3 months. However, we observed only failure to these therapies. At this juncture, he was started on ART (Zidovudine, Lamivudine, and Nevirapine) since his CD4 count was 253 cells/mm^3 at that time. Skin lesions completely disappeared within 6 months of ART [Figure 5]. It was a miraculous response to ART. The patient is being followed up till date. His CD4 count as on December 2015 was 390 cells/mm^3.

DISCUSSION

BD is a form of SCC *in situ* originally described in 1912 by Bowen, a Boston dermatologist.[2]

BD may occur at any age in adults but more common in individuals older than 60 years of age with a slight preponderance in women.[3] It is commonly located on the lower limbs, head, and neck. However, BD is also seen in subungual or periungual, palmar, genital, and perianal areas. Usually, BD is a solitary lesion, but in 10-20%, it occurs at multiple sites.[4]

Several etiological factors of BD have been reported, such as irradiation (ultraviolet irradiation, radiotherapy, and photochemotherapy), carcinogens (e.g., arsenic), immunosuppression (e.g., after organ transplantation, AIDS), viral (strong association of perianal and genital lesions with human papilloma-virus, especially [HPV] 16; 47% of acral and 24% of nonacral extragenital BD contain HPV genome), and some others such as chronic injury, or dermatoses.[5,6]

Multiple lesions of BD are mostly seen in individuals exposed to arsenic. Arsenic exposure toxicity due to several medications has been reported in the past.[7,8]

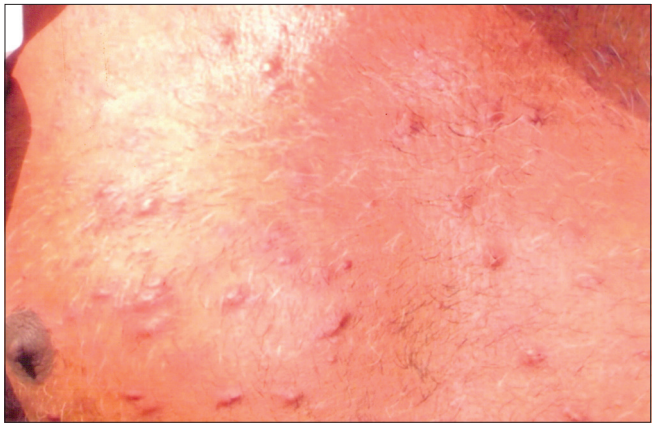

Figure 1: Reddish-brown-papular and nodular lesions in the chest wall

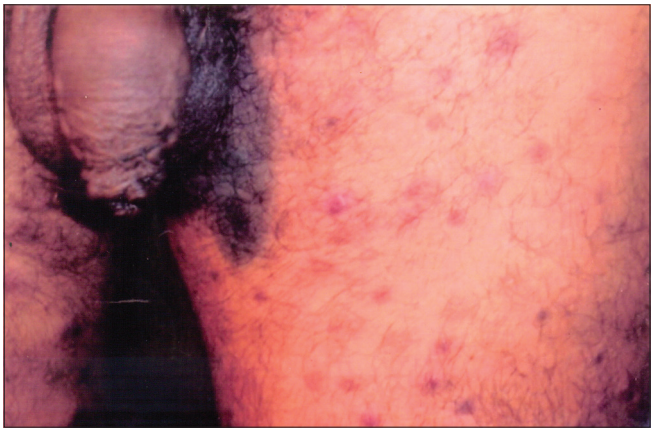

Figure 2: Reddish-brown-papular and nodular lesions over thigh

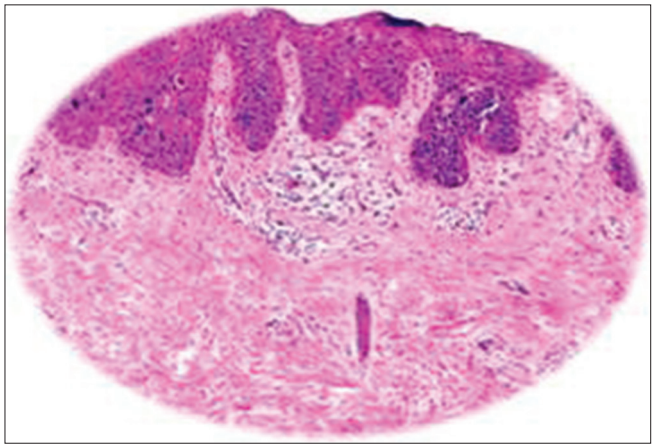

Figure 3: Hyperkeratosis, marked acanthosis with intact basement membrane. (H and E, ×40)

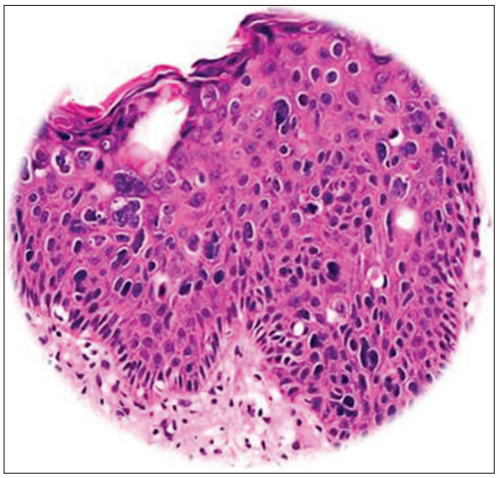

Figure 4: Atypical dyskeratotic cells with hyperchromatic nucleus and intact basement membrane. (H and E, ×100)

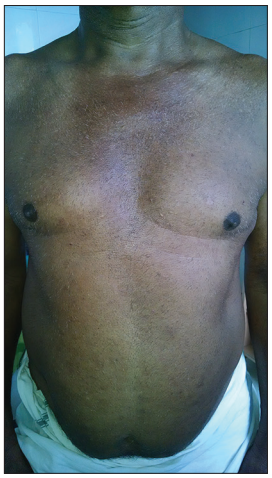

Figure 5: Clearance of the lesions after treatment

Our case had no occupational exposure suggestive of arsenic toxicity in the past. It is possible that long-term Siddha medication could be the reason in our patient. However, this could not be confirmed due to the lack of availability of Siddha medication which he had ingested in the past. The estimation of blood arsenic level was futile because it tends to normalize within a short span of 6 months after nil arsenic exposure.[9] It is known that gradual improvement occurs in signs of chronic arsenicism over a period of 18 months if no further exposure to arsenic occurs.[9] However, diffuse pigmentation may remain in such patients.[9] Clinically arsenical BD can be differentiated from nonarsenical BD by its multiple and recrudescent lesions, occurring mainly on sun-protected areas of skin. However, we are not able to confirm that arsenic could be the reason for multiple BD in our case.

Clinically, a typical BD presents as discrete, slowly enlarging, well-demarcated erythematous thin plaque, with well-demarcated, irregular borders, and overlying crusts. The clinical variants of BD include erythematous type, hyperkeratotic type, pigmented type, intertriginous type, and subungual or periungual type. Clinically, it should be differentiated from actinic keratosis, irritated seborrheic keratosis, lichen planus, psoriasis, amelanotic melanoma, superficial basal cell carcinoma, viral warts, and SCC.

HPE is important for absolute diagnosis which shows full-thickness involvement of the epidermis, and sometimes, the pilosebaceous epithelium, by atypical keratinocytes. This is associated with disorderly maturation of the epidermis, mitoses at different levels, multinucleate keratinocytes, and dyskeratotic cells. Throughout the epidermis, the cells lie in complete disorder, resulting in a "windblown appearance". Usually, there is a loss of the granular layer, with overlying parakeratosis and, sometimes, hyperkeratosis with intact basement membrane. In some cases, the proliferating cells may be surrounded by relatively normal epidermal cells to give a characteristic "Borst-Jadassohn" appearance.[10]

The histological variants of BD includes psoriasiform type, atrophic type, verrucous-hyperkeratotic type, papillated variant, irregular variant, pigmented type, and pagetoid type. Histopathologically, BD must be differentiated from bowenoid actinic keratosis, Paget's disease, pagetoid melanoma *in situ*, and bowenoid papulosis. No histologic difference exists between bowenoid actinic keratosis and BD. They may differ merely in size, with the bowenoid actinic keratosis usually being smaller than BD. Pagetoid variant of BD is sometimes difficult to distinguish from Paget's disease and from *in situ* superficial spreading melanoma.[11] However, in Paget's disease, there will not be any dyskeratotic cells like BD. Melanoma cells are positive for S100 proteins, whereas Paget cells usually demonstrate carcinoembryonic antigen.[11]

There is a wide range of therapeutic options available for the treatment of BD including cryotherapy, curettage, cautery, photo-dynamic therapy, laser destruction, excision, 5-fluorouracil cream, imiquimod cream, and radiotherapy.[6] Early diagnosis carries a better prognosis. The patients should be followed up till life.

CONCLUSION

We are presenting this case for its rare occurrence. To the best of our knowledge, this happens to be the first case of BD in an HIV-positive individual which cleared miraculously with ART.

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Conflicts of interest

There are no conflicts of interest.

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Luc Antoine Montagnier (born 18 August 1932) is a French virologist and joint recipient with Françoise Barré-Sinoussi and HaraldzurHausen of the 2008 Nobel Prize in Physiology or Medicine for his discovery of the human immunodeficiency virus (HIV).[1] A long-time researcher at the Pasteur Institute in Paris, he currently works as a full-time professor at Shanghai Jiao Tong University in China.

He was born on 18th August 1932 in Chabris, a French town..

Montagnier is the co-founder of the World Foundation for AIDS Research and Prevention and co-directs the Program for International Viral Collaboration. He is the founder and a former president of the Houston-based World Foundation for Medical Research and Prevention.